determined by BIACORE® analysis). In some aspects, the ActRIIB- and ActRIIA-binding protein has 2, 3, or 4 of the above characteristics. In some aspects, the ActRIIB- and ActRIIA-binding protein has at least 2 or at least 3 of the above characteristics. In further aspects, the ActRIIB-binding protein competes for binding to ActRIIB and ActRIIA with an antibody having an ActRIIB- and ActRIIA binding VH and VL pair disclosed herein. In further aspects, the ActRIIB- and ActRIIA-binding protein is an anti-ActRIIB and ActRIIB antibody or an ActRIIB- and ActRIIB binding antibody fragment.

[0010] In some aspects, the ActRII-binding protein specifically binds ActRIIA. In further aspects, the provided ActRII-binding protein specifically binds ActRIIA and has at least one characteristic selected from the group consisting of: (a) competes with an ActRII ligand (e.g., activin A, activin B, GDF1, GDF3, GDF8 (myostatin), GDF11, BMP6, BMP7, BMP9, or BMP10) for binding to ActRIIA; (b) decreases the phosphorylation of ALK4 and/or ALK7 in cells expressing ActRIIA and ALK4 and/or ALK7 in the presence of an ActRIIA ligand (e.g., activin A and/or GDF8 (myostatin)); (c) decreases the phosphorylation of Smads (e.g., Smad2 and/or Smad3) in cells expressing ActRIIA in the presence of an ActRIIA ligand (e.g., activin A and/or GDF8); and (d) binds to ActRIIA with a K_D of ≤1 nM and ≥1 pM (e.g., as determined by BIACORE® analysis). In some aspects, the ActRIIA-binding protein has 2, 3, or 4 of the above characteristics. In some aspects, the ActRIIA-binding protein has at least 2 or at least 3 of the above characteristics. In further aspects, the ActRIIA-binding protein competes for binding to ActRIIA with an antibody having an ActRIIA-binding VH and VL pair disclosed herein. In further aspects, the ActRIIA-binding protein is an anti-ActRIIA antibody or an ActRIIA-binding antibody fragment.

[0011] In some aspects, the ActRII-binding protein comprises a set of complementary determining regions (CDRs): heavy chain variable region (VH)-CDR1, VH-CDR2, VH-CDR3, light chain variable region (VL)-CDR1, VL-CDR2 and VL-CDR3, wherein the CDRs are present in a heavy chain variable region (VH) and a light chain variable region (VL) pair disclosed in Table 1. In some aspects, the ActRII-binding protein comprises a set of CDRs present in a VH and a VL pair selected from the group consisting of: (a) a VH sequence of SEQ ID NO:2, 16, 22, 28, 34, or 40, and a VL sequence of SEQ ID NO:9, and wherein the protein binds ActRIIB, (b) a VH sequence of SEQ ID NO:63 or 77, and a VL having the amino acid sequence of SEQ ID NO:70, and wherein the protein binds ActRIIB; (c) a VH sequence of SEQ ID NO:45 or 57, and a VL sequence of SEQ ID NO:50, and wherein the protein binds ActRIIB; (d) a VH sequence of SEQ ID NO:84, 98, 105, 112, or 119, and a VL sequence of SEQ ID NO:91, and wherein the protein binds and ActRIIB and activin receptor type IIA (ActRIIA), and (e) a VH sequence of SEQ ID NO:125, and a VL sequence of SEQ ID NO:132, and wherein the protein binds ActRIIA.

[0012] In some aspects, the ActRII-binding protein comprises a set of CDRs present in a VH having the amino acid sequence of SEQ ID NO:144 and a VL having the amino acid sequence of SEQ ID NO:151, and wherein the protein binds ActRIIB.

[0013] In some aspects, the ActRII-binding protein comprises a set of CDRs present in a VH having the amino acid sequence of SEQ ID NO:165 and a VL having the amino acid sequence of SEQ ID NO:172, and wherein the protein binds ActRIIA and ActRIIB.

[0014] In additional aspects, the ActRII-binding protein specifically binds ActRII and comprises a set of CDRs: VH-CDR1, VH-CDR2, VH-CDR3, VL-CDR1, VL-CDR2, and VL-CDR3, wherein the set of CDRs is identical to, or has a total of one, two, three, four, five, six, seven, eight, nine, ten, or fewer than ten, amino acid substitutions, deletions, and/or insertions from a reference set of CDRs in which: (a)(i) VH-CDR1 has the amino acid sequence of SEQ ID NO:3, 17, 23, 29, 35 or 41; (ii) VH-CDR2 has the amino acid sequence of SEQ ID NO:4, 18, 24, 30, 178, or 36; (iii) VH-CDR3 has the amino acid sequence of SEQ ID NO:5; (iv) VL-CDR1 has the amino acid sequence of SEQ ID NO:10; (v) VL-CDR2 has the amino acid sequence of SEQ ID NO:11; and (vi) VL-CDR3 has the amino acid sequence of SEQ ID NO:12; and wherein the protein binds ActRIIB; (b)(i) VH-CDR1 has the amino acid sequence of SEQ ID NO:64 or 78; (ii) VH-CDR2 has the amino acid sequence of SEQ ID NO:65 or 79; (iii) VH-CDR3 has the amino acid sequence of SEQ ID NO:66 or 80; (iv) VL-CDR1 has the amino acid sequence of SEQ ID NO:71; (v) VL-CDR2 has the amino acid sequence of SEQ ID NO:72; and (vi) VL-CDR3 has the amino acid sequence of SEQ ID NO:73; and wherein the protein binds ActRIIB; (c)(i) VH-CDR1 has the amino acid sequence of SEQ ID NO:3 or 58; (ii) VH-CDR2 has the amino acid sequence of SEQ ID NO:4 or 59; (iii) VH-CDR3 has the amino acid sequence of SEQ ID NO:46; (iv) VL-CDR1 has the amino acid sequence of SEQ ID NO:51; (v) VL-CDR2 has the amino acid sequence of SEQ ID NO:52; and (vi) VL-CDR3 has the amino acid sequence of SEQ ID NO:53; and wherein the protein binds ActRIIB; (d)(i) VH-CDR1 has the amino acid sequence of SEQ ID NO:85, 99, 106, 166, or 113; (ii) VH-CDR2 has the amino acid sequence of SEQ ID NO:86, 100, 107, 114, 167, or 120; (iii) VH-CDR3 has the amino acid sequence of SEQ ID NO:87, 101, 108, 115, 168, or 121; (iv) VL-CDR1 has the amino acid sequence of SEQ ID NO:92, or 173; (v) VL-CDR2 has the amino acid sequence of SEQ ID NO:93, 153, or 174; and (vi) VL-CDR3 has the amino acid sequence of SEQ ID NO:94, or 175; and wherein the protein binds ActRIIB and ActRIIA; or (e)(i) VH-CDR1 has the amino acid sequence of SEQ ID NO:126; (ii) VH-CDR2 has the amino acid sequence of SEQ ID NO:127; (iii) VH-CDR3 has the amino acid sequence of SEQ ID NO:128; (iv) VL-CDR1 has the amino acid sequence of SEQ ID NO:133; (v) VL-CDR2 has the amino acid sequence of SEQ ID NO:134; and (vi) VL-CDR3 has the amino acid sequence of SEQ ID NO:135; and wherein the protein binds ActRIIA.

[0015] In additional aspects, the ActRII-binding protein specifically binds ActRIIB and comprises a set of CDRs: VH-CDR1, VH-CDR2, VH-CDR3, VL-CDR1, VL-CDR2, and VL-CDR3, wherein the set of CDRs is identical to, or has a total of one, two, three, four, five, six, seven, eight, nine, ten, or fewer than ten, amino acid substitutions, deletions, and/or insertions from a reference set of CDRs in which (i) VH-CDR1 has the amino acid sequence of SEQ ID NO:145; (ii) VH-CDR2 has the amino acid sequence of SEQ ID NO:146; (iii) VH-CDR3 has the amino acid sequence of SEQ ID NO:147; (iv) VL-CDR1 has the amino acid sequence of SEQ ID NO:152; (v) VL-CDR2 has the amino acid sequence of SEQ ID NO:153; and (vi) VL-CDR3 has the amino acid sequence of SEQ ID NO:154.